

CLAIMS READABLE OF ELECTED SPECIES

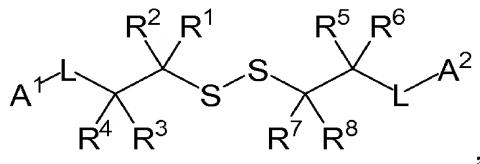
In the claims, please amend claims 7 and 19 as follows:

1-6. (canceled)

7. (currently amended) A disulfide bond-containing crosslinking agent comprising:

- a) a disulfide bond;
- b) at least one electron withdrawing group wherein proximity of said electron withdrawing group to said disulfide bond results in said disulfide bond being cleaved more rapidly than oxidized glutathione; and,
- c) two reactive groups independently selected from the group consisting of: ~~acid halide, O acyl urea, N hydroxysuccinimide esters, succinimide esters, p nitrophenyl ester, o nitrophenyl ester, pentachlorophenyl ester, pentafluorophenyl ester, carbonyl imidazole, carbonyl pyridinium, carbonyl dimethylaminopyridinium, amide, maleimide, urea, sulfonyl chloride, aldehyde, ketone, epoxide, carbonate, imidoester, activated carboxylate, acryloyl derivative, primary amine, aziridine derivative, carbamate, diol, hydrozide derivative~~ and anhydride, wherein:
  - i) one reactive group is located on each side of said disulfide bond, but not between said electron withdrawing group and said disulfide bond;
  - ii) said reactive groups are capable of forming covalent bonds with separate compounds on each side of said disulfide bond;
  - iii) formation of said covalent bonds does not result in loss of said electron withdrawing group, cleavage of said disulfide bond, or said disulfide bond not being cleaved more rapidly than oxidized glutathione; and,
  - iv) subsequent cleavage of said disulfide bond results in the formation of two molecules.

8. (previously presented) The disulfide bond-containing crosslinking agent of claim 7 wherein disulfide bond-containing crosslinking agent consists of the structure selected from the group consisting of:



wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, and R<sup>8</sup> are independently selected from the group consisting of: hydrogen, alkyl, alkenyl, alkynyl, aralkyl, aralkenyl, or aralkynyl, heteroatom (N, O, S), carbonyl group, and electron withdrawing group, at least one of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, or R<sup>8</sup> consists of an electron withdrawing group, X consists of a heteroatom selected from the group including sulfur, oxygen, nitrogen, and phosphorus, L consists of a linker group that provides a connection between the disulfide bond and the reactive groups, and A<sup>1</sup> and A<sup>2</sup> are reactive groups.

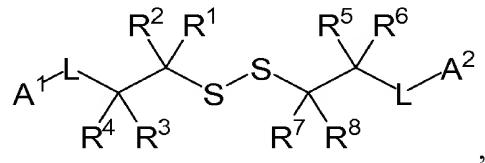
9-11. (canceled)

12-18. (canceled)

19. (currently amended) A disulfide bond-containing crosslinking agent comprising:

- a) a disulfide bond;
- b) at least one electron withdrawing group wherein proximity of said electron withdrawing group to said disulfide bond reduces the pKa of at least one of the constituent thiols of said disulfide bond to less than glutathione thiol pKa; and,
- c) two reactive groups independently selected from the group consisting of: isothiocyanate, isocyanate, acyl azide, ~~acid halide, O acyl urea, N hydroxysuccinimide esters, succinimide esters, p nitrophenyl ester, o nitrophenyl ester, pentachlorophenyl ester, pentafluorophenyl ester, carbonyl imidazole, carbonyl pyridinium, carbonyl dimethyl aminopyridinium, amide, maleimide, urea, sulfonyl chloride, aldehyde, ketone, epoxide, carbonate, imidoester, activated carboxylate, acryloyl derivative, primary amine, aziridine derivative, carbamate, diol, hydrozide derivative and anhydride,~~ wherein:
  - i) one reactive group is located on each side of said disulfide bond, but not between said electron withdrawing group and said disulfide bond;
  - ii) said reactive groups are capable of forming covalent bonds with separate compounds on each side of said disulfide bond;
  - iii) formation of said covalent bonds does not result in loss of said electron withdrawing group, cleavage of said disulfide bond, or an increase in the pKa of at least one of the constituent thiols of the disulfide bond such that said pKa is not less than glutathione thiol pKa; and,
  - iv) subsequent cleavage of said disulfide bond results in the formation of two molecules.

20. (previously presented) The disulfide bond-containing crosslinking agent of claim 19 wherein disulfide bond-containing crosslinking agent consists of the structure selected from the group consisting of:



wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$ ,  $\text{R}^6$ ,  $\text{R}^7$ , and  $\text{R}^8$  are independently selected from the group consisting of: hydrogen, alkyl, alkenyl, alkynyl, aralkyl, aralkenyl, or aralkynyl, heteroatom (N, O, S), carbonyl group, and electron withdrawing group, at least one of  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$ ,  $\text{R}^5$ ,  $\text{R}^6$ ,  $\text{R}^7$ , or  $\text{R}^8$  consists of an electron withdrawing group, X consists of a heteroatom selected from the group including sulfur, oxygen, nitrogen, and phosphorus, L consists of a linker group that provides a connection between the disulfide bond and the reactive groups, and  $\text{A}^1$  and  $\text{A}^2$  are reactive groups.

21-23. (canceled)

24-28. (canceled)

Remarks

Rejection of the claims under 35 USC §102:

Claims 7, 8, 19, and 20 have been rejected under 35 U.S.C. 102(b) as being anticipated by Abderhalden et al. (Berichte der Deutschen Chemischen Gesellschaft 1916). Applicants have amended the claims to obviate the rejection. Specifically, Applicants have amended claims 7 and 19 to delete the term “amide”. In view of the amendment, Applicants request reconsideration of this §102 rejection.

Support for physiological conditions can be found in the specification on page 1 lines 28-29, page 3 lines 6-11 and 21-26, page 4 lines 24-27. In agreement with Applicants’ and accepted use of the term, Merriam-Webster defines physiological as: characteristic of or appropriate to an organism's healthy or normal functioning.

Support for activated carboxylate can be found in the specification on page 6 lines 16-27, page 8 line 26 to page 9 line 4, page 11 lines 4-15, page 13 lines 17-28, page 15 line 28 to page 16 line 7, page 18 lines 7-18, and page 32 lines 17-26.

Support for acryloyl derivative can be found in the specification on page 6 lines 24-27.

Support for primary amine can be found in the specification on page 7 lines 1-4. Applicants note that the structure disclosed by Abderhalden et al. further contains a primary amine group. However, the structure disclosed by Abderhalden does not contain “at least one electron withdrawing group wherein proximity of said electron withdrawing group to said disulfide bond results in said disulfide bond being cleaved more rapidly than oxidized glutathione in physiological conditions”. Applicants have provided, with this amendment, a declaration under 37 C.F.R. 1.132 showing that the Abderhalden et al. compound does not contain a disulfide bond that is cleaved more rapidly than oxidized glutathione or have a pKa of at least one of the constituent thiols that is less than glutathione thiol pKa.

Support for aziridine derivative can be found in the specification on page 6 lines 24-27.

Support for carbamate can be found in the specification on page 21 line 32 to page 22 line 2.

Support for diol can be found in the specification on page 6 lines 11-14.

Support for hydrozide derivative can be found in the specification on page 7 lines 1-4

The Examiner's rejections are now believed to be overcome by this response to the Office Action. In view of Applicants' amendment and arguments, it is submitted that claims 7, 8, 19, and 20 should be allowable.

Respectfully submitted,

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I hereby certify that this correspondence is being transmitted to the USPTO on this date: August 13, 2008.

/Kirk Ekena/  
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